

Complete Summary

GUIDELINE TITLE

Practice guideline for the treatment of patients with Alzheimer's disease and other dementias of late life.

BIBLIOGRAPHIC SOURCE(S)

American Psychiatric Association (APA). Practice guideline for the treatment of patients with Alzheimer's disease and other dementias of late life. Am J Psychiatry 1997 May; 154(5 Suppl): 1-39. [243 references] [PubMed](#)

American Psychiatric Association (APA). Practice guidelines for the treatment of patients with Alzheimer's disease and other dementias of late life. Washington (DC): American Psychiatric Press, Inc.; 1997 May. 93 p. [243 references]

GUIDELINE STATUS

This is the current release of the guideline.

According to the guideline developer, this guideline is still considered to be current as of December 2004, based on a review of literature published since the original guideline publication.

In addition, a Guideline Watch, which summarizes significant developments in practice since the publication of the original guideline, was published in August 2004 and is available from the [American Psychiatric Association Web site](#) (see also the "Availability of Companion Documents" field below).

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- On April 12, 2005, the U.S. Food and Drug Administration (FDA) issued a public health advisory to alert health care providers, patients, and patient caregivers to new safety information concerning an unapproved, "off-label" use of certain antipsychotic drugs approved for the treatment of schizophrenia and mania. FDA has determined that the treatment of behavioral disorders in elderly patients with dementia with atypical (second generation) antipsychotic medications is associated with increased mortality. Clinical studies of these drugs in this population have shown a higher death

- rate associated with their use compared to patients receiving a placebo. See the [FDA Web site](#) for more information.
- On July 1, 2005, in response to recent scientific publications that report the possibility of increased risk of suicidal behavior in adults treated with antidepressants, the U.S. Food and Drug Administration (FDA) issued a Public Health Advisory to update patients and healthcare providers with the latest information on this subject. Even before the publication of these recent reports, FDA had already begun the process of reviewing available data to determine whether there is an increased risk of suicidal behavior in adults taking antidepressants. The Agency has asked manufacturers to provide information from their trials using an approach similar to that used in the evaluation of the risk of suicidal behavior in the pediatric population taking antidepressants. This effort will involve hundreds of clinical trials and may take more than a year to complete. See the [FDA Web site](#) for more information.
 - On January 13, 2006, Novartis and the U.S. Food and Drug Administration (FDA) notified healthcare professionals of revisions to the BOXED WARNING, WARNINGS, CONTRAINDICATIONS, PRECAUTIONS (Information for Patients and Pharmacokinetic-Related Interactions subsections), and ADVERSE REACTIONS (Postmarketing Clinical Experience subsection) sections of the prescribing information for Clozaril (clozapine) tablets. Recommendations from the FDA's Psychopharmacological Drugs Advisory Committee regarding the white blood cell monitoring schedule, required for all clozapine users, has resulted in modification in the monitoring schedule. Additional labeling changes address safety issues related to dementia-related psychosis, paralytic ileus, hypercholesterolemia and pharmacokinetic interaction with citalopram. See the [FDA Web site](#) for more information.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **

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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

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SCOPE

DISEASE/CONDITION(S)

- Alzheimer's disease
- Other dementias of late life, including:
 - Vascular dementia
 - Parkinson's disease
 - Lewy body disease

- Pick's and other frontal lobe dementias

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Neurology
Psychiatry

INTENDED USERS

Allied Health Personnel
Physicians

GUIDELINE OBJECTIVE(S)

- To assist physicians in clinical decision-making
- To improve patient care for Alzheimer's disease by incorporating the principles of the guideline into individual practices
- To assist psychiatrists in caring for demented patients
- To advance clinical knowledge and enrich and expand the skills of psychiatrists

TARGET POPULATION

Patients with dementia of the Alzheimer's type and other dementias associated with aging, including vascular (multi infarct) dementia, Parkinson's disease, Lewy body disease, and Pick's and other frontal lobe dementias.

The guideline does cover dementias associated with general medical conditions, such as Huntington's disease, head trauma, structural lesions, or endocrine and metabolic disturbances. However, while many of the research data on which the recommendations are based come from the study of Alzheimer's disease and to a lesser extent, vascular dementia, many of the recommendations regarding the management of cognitive and functional changes and behavioral complications apply to dementia in general.

INTERVENTIONS AND PRACTICES CONSIDERED

Psychiatric Management; Psychotherapy and Other Psychosocial Treatments

1. Diagnostic evaluation and referral for any needed general medical care: The evaluation at a minimum should include a clear history of the onset and progression of symptoms; a complete physical and neurological examination; a psychiatric examination, including a cognitive evaluation, e.g., the Mini-Mental State examination; a review of the patient's medications; and laboratory studies, i.e., complete blood count (CBC), blood chemistry battery

(including glucose, electrolytes, calcium, and kidney and liver function tests), measurement of vitamin B₁₂ level, syphilis serology, and thyroid function tests.

2. An assessment for past or current psychiatric illness, such as schizophrenia or major depression that might mimic or exacerbate the dementia.
3. For some patients, toxicology studies, erythrocyte sedimentation rate, HIV testing, a lumbar puncture, or an electroencephalogram are indicated.
4. If the history and neurological examination suggest an early onset, rapid or atypical course or possible focal lesion, a structural imaging study, with computerized tomography (CT) or magnetic resonance imaging (MRI), should be obtained.
5. Functional imaging techniques, such as positron emission tomography (PET) and single photon emission computed tomography (SPECT), have not yet shown clinical utility but are the focus of current study. Testing for the apolipoprotein E-4 gene (APOE-4) is not currently recommended for routine use in diagnosis because it is found in many nondemented elderly and is not found in many patients with dementia.

Specific Psychotherapies/Psychosocial Treatments

1. Behavior-oriented approaches
2. Emotion-oriented approaches: including supportive psychotherapy, reminiscence therapy, validation therapy, sensory integration, and simulated presence therapy
3. Cognition-oriented approaches: including reality orientation and skills training
4. Stimulation-oriented approaches: including activities or recreational therapies (e.g., music, dance, art)

Somatic Treatments

1. Treatments for cognitive and functional losses
 - Cholinesterase inhibitors (tacrine and donepezil)
 - α -tocopherol (vitamin E)
 - Selegiline (deprenyl), approved for Parkinson's disease but studies and used in dementia
 - Ergoloid mesylates (Hydergine), which are approved for nonspecific cognitive decline
 - Agents proposed for the treatment of cognitive decline and dementia, but for which adequate data are lacking, including: aspirin and other NSAIDs (non-steroidal anti-inflammatory drugs), estrogen supplementation, melatonin, botanical agents (e.g., ginkgo biloba), and chelating agents (e.g., desferioxamine)
2. Treatments for psychosis and agitation
 - Antipsychotic medications: including conventional antipsychotics; and newer agents such as risperidone, clozapine, olanzapine, and quetiapine.
 - Anticonvulsants: carbamazepine and valproate
 - Benzodiazepines: including long-acting agents (e.g., 12 mg/day diazepam, and clonazepam) and the shorter-acting agents more commonly used today (oxazepam, lorazepam, and temazepam) are occasionally effective but have greater risks.

- Other agents for the treatment of agitation in patients with dementia, for which adequate data are lacking, including: trazodone, SSRIs (selective serotonin reuptake inhibitors), buspirone, medroxyprogesterone and related hormonal agents (for male patients displaying intrusive disinhibited sexual behavior, a particular problem in patients with frontal lobe dementias), lithium carbonate because of its occasional utility for mentally retarded patients, beta blockers (notably propranolol, metoprolol, and pindolol).
3. Treatments for depression
 - Antidepressants: including typical antidepressants (cyclic antidepressants, SSRIs, and MAOIs [monoamine oxidase inhibitors]); imipramine, dopaminergic agents such as psychostimulants (d-amphetamine, methylphenidate); amantadine, bromocriptine.
 - Electroconvulsive therapy (ECT)
 4. Treatments for sleep disturbance are not well established. Suggested options include:
 - Antidepressants with sedative properties (trazodone, nortriptyline)
 - Zolpidem
 - Antipsychotics (haloperidol, thioridazine, mesoridazine)
 - Benzodiazepines (e.g., lorazepam)
 - Bright light therapy
 - Chloral hydrate
 - Triazolam
 - Tryptophan

MAJOR OUTCOMES CONSIDERED

- Morbidity and mortality associated with Alzheimer's disease and other dementias of late life
- Level of cognitive performance
- Patient's level of function (activities of daily living)
- Patient comfort
- Disruption to families and caregivers

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The following computerized searches of relevant literature were conducted using Excerpta Medica and MEDLINE for the period 1966 to 1994. The primary search was done in three parts:

1. medication treatment of dementia and complications (except depression)
2. nonmedication treatment of dementia and complications (except depression), and
3. treatment of depression in dementia

In addition to this primary search, additional searches were performed where there did not appear to be adequate coverage, as follows. The key words used in Excerpta Medica searches for the period 1991-1995 were all terms indexed under "dementia", "alzheimer's", "hydergine", and "tacrine". These terms resulted in 376 citations. The key words used in MEDLINE searches were "chloral hydrate in treatment for dementia", "valproic acid in treatment for agitation", "lithium in treatment for agitation", "carbamazepine in treatment for agitation", and "beta blockers in treatment for agitation" for the period 1966-1995; "driving and dementia" for the period 1990-1995; and "MAO-inhibitors" with all terms indexed under "dementia" and "alzheimer's", all terms indexed under "dihydroergotoxine", all terms relevant for "tacrine", "NSAIDS in treatment of cognition disturbance", "estrogen in the treatment of cognition disorders", "chelation therapy in the treatment of cognition disorders", "day care-respite care-non-institutional treatment in dementia", and "zolpidem in the treatment of dementia or cognition" for the period 1991-1995.

NUMBER OF SOURCE DOCUMENTS

376 source documents were retrieved by the Excerpta Medica searches for the period 1991-1995; where key words used were all terms indexed under "dementia", "alzheimer's", "hydergine", and "tacrine".

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Once a topic is chosen for guideline development, a work group is formed to draft the guideline. By design, the work group consists of psychiatrists in active clinical practice with diverse expertise and practice experience relevant to the topic. Policies established by the Steering Committee guide the work of systematically reviewing data in the literature and forging consensus on the implications of those

data, as well as describing a clinical consensus. These policies, in turn, stem from criteria formulated by the American Medical Association to promote the development of guidelines that have a strong evidence base and that make optimal use of clinical consensus.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Each recommendation is identified as falling into one of three categories of endorsement, indicated by a bracketed Roman numeral following the statement. The three categories represent varying levels of clinical confidence regarding the recommendation:

[I] Recommended with substantial clinical confidence.

[II] Recommended with moderate clinical confidence.

[III] May be recommended on the basis of individual circumstances.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Multiple drafts were produced with widespread review and comments by 10 organizations and over 48 individuals, followed by approval by the APA Assembly and Board of Trustees.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from APA: The following summary is intended to provide an overview of the organization and scope of recommendations in the full-text practice guideline. The treatment of patients with Alzheimer's disease and related dementias requires the consideration of many factors and cannot adequately be reviewed in a brief summary. The reader is encouraged to consult the relevant portions of the full-text guideline when specific treatment recommendations are sought. This summary is not intended to stand by itself.

Each recommendation is identified as falling into one of these three categories of endorsement, indicated by a bracketed Roman numeral following the statement. The three categories represent varying levels of clinical confidence:

[I] recommended with substantial clinical confidence

[II] recommended with moderate clinical confidence

[III] may be recommended on the basis of individual circumstances

GENERAL TREATMENT PRINCIPLES AND ALTERNATIVES

Patients with dementia display a broad range of cognitive impairments, behavioral symptoms, and mood changes. As a result, they require an individualized and multimodal treatment plan. Dementia is often progressive; thus, treatment must evolve with time in order to address newly emerging issues. At each stage the psychiatrist should be vigilant for symptoms likely to be present and should help the patient and family anticipate future symptoms and the care likely to be required [I].

1. Psychiatric management

The core of the treatment of demented patients is psychiatric management, which must be based on a solid alliance with the patient and family and thorough psychiatric, neurological, and general medical evaluations of the nature and cause of the cognitive deficits and associated noncognitive symptoms [I]. It is particularly critical to identify and treat general medical conditions that may be responsible for or contribute to the dementia or associated behavioral symptoms [I].

Ongoing assessment should include periodic monitoring of the development and evolution of cognitive and noncognitive psychiatric symptoms and their response to intervention [I]. In order to offer prompt treatment, assure safety, and provide timely advice to the patient and family, it is generally necessary to see patients in routine follow-up every 4-6 months [II]. More frequent visits (e.g., once or twice a week) may be required for patients with complex or potentially dangerous symptoms or during the administration of specific therapies [I]. Safety measures include evaluation of suicidality and the potential for violence; recommendations regarding adequate supervision, preventing falls, and limiting the hazards of wandering; vigilance regarding neglect or abuse; and restrictions on driving and use of other dangerous equipment [I]. Driving poses particular concern because of its public health impact. All patients and families should be informed that even mild dementia increases the risk of accidents [I]. Mildly impaired patients should be urged to stop driving or limit their driving to safer situations [II], and moderately and severely impaired patients should be advised not to drive [II]; in both cases, the advice should be given to the family as well as the patient [I]. Another critical aspect of psychiatric management is educating the patient and family about the illness, its treatment, and available sources of care and support (e.g., support groups, various types of respite care, nursing homes and other long-term care facilities, the Alzheimer's Association). It is also important to help patients and their families plan for financial and legal issues due to the patient's incapacity (e.g.,

power of attorney for medical and financial decisions, an up-to-date will, the cost of long-term care) [I].

2. Specific psycho-therapies and other psychosocial treatments

In addition to the psychosocial interventions subsumed under psychiatric management, a number of specific interventions are appropriate for some patients with dementia. Few of these treatments have been subjected to double-blind, randomized evaluation, but some research, along with clinical practice, supports their effectiveness. Behavior-oriented treatments identify the antecedents and consequences of problem behaviors and institute changes in the environment that minimize precipitants and/or consequences. These approaches have not been subjected to randomized clinical trials but are supported by single-case studies and are in widespread clinical use [II]. Stimulation-oriented treatments, such as recreational activity, art therapy, and pet therapy, along with other formal and informal means of maximizing pleasurable activities for patients, have modest support from clinical trials for improving function and mood, and common sense supports their use as part of the humane care of patients with dementia [II]. Among the emotion-oriented treatments, supportive psychotherapy is used by some practitioners to address issues of loss in the early stages of dementia, reminiscence therapy has some modest research support for improvement of mood and behavior, while validation therapy and sensory integration have less research support; none of these modalities has been subjected to rigorous testing [III]. Cognition-oriented treatments, such as reality orientation, cognitive retraining, and skills training, are focused on specific cognitive deficits, are unlikely to be beneficial, and have been associated with frustration in some patients [III].

3. Special concerns regarding somatic treatments for elderly and demented patients

Psychoactive medications are effective in the management of some symptoms associated with dementia, but they must be used with caution [I]. Elderly individuals have decreased renal clearance and slowed hepatic metabolism of many medications, so lower starting doses, smaller increases in dose, and longer intervals between increments must be used [I]. General medical conditions and other medications may further alter the binding, metabolism, and excretion of many medications [I]. In addition, the elderly and patients with dementia are more sensitive to certain medication side effects, including anticholinergic effects, orthostasis, central nervous system (CNS) sedation, and parkinsonism [I]. For all of these reasons, medications should be used with considerable care, particularly when more than one agent is being used [I].

4. Treatment of cognitive symptoms

The available treatments for the cognitive symptoms of dementia are limited. Two cholinesterase inhibitors are available for Alzheimer's

disease: tacrine and donepezil. Either may be offered to patients with mild to moderate Alzheimer's disease after a thorough discussion of its potential risks and benefits [I]. Tacrine has been shown to lead to modest improvements in cognition in a substantial minority of patients, but up to 30% of patients cannot tolerate the medication because of nausea and vomiting or substantial (but reversible) elevations in liver enzyme levels [I]. Donepezil has also been shown to lead to modest improvements in a substantial minority of patients, and it appears to have a similar propensity to cause nausea and vomiting [II]. Because donepezil does not share tacrine's risk for liver toxicity, and thus does not require frequent monitoring, it may prove preferable as a first-line treatment [III]. However, accumulated data from additional clinical trials and clinical practice will be necessary in order to establish a more complete picture of its efficacy and side effect profile.

Vitamin E may also be considered for patients with moderate Alzheimer's disease to slow the rate of [I], and might also be beneficial earlier or later in the course of the disease [III]. A single large well-conducted trial of vitamin E showed a significant delay in poor outcome over a 2-year period [I], and the agent appears to be very safe [I]. Thus, it might be considered alone or in combination with a cholinesterase inhibitor in the treatment of Alzheimer's disease [II]. Its role in the treatment of other dementing disorders is unknown.

Selegiline may also be considered for patients with moderate Alzheimer's disease to prevent further decline [II], and may possibly be beneficial earlier or later in the course of the disease [III]. A single large well-conducted trial showed a significant delay in poor outcome over a 2-year period [I]. However, selegiline is associated with orthostatic hypotension and a risk for medication interactions, so vitamin E, which appeared equally efficacious in a direct comparison, may be preferable [II]. However, because limited evidence suggests that selegiline may offer short-term improvement in dementia, it might be appropriate as an alternative to cholinesterase inhibitors in patients who are ineligible for, intolerant of, or unresponsive to these agents [III]. Because there was no evidence of an additive effect of vitamin E and selegiline, there is no empirical basis for using the two agents in combination [I]. The effect of selegiline in combination with cholinesterase inhibitors is unknown.

The mixture of ergot mesylates known by the trade name Hydergine cannot be recommended for the treatment of cognitive symptoms but may be offered to patients with vascular dementia and may be appropriately continued for patients who experience a benefit [III]. This agent has been assessed in a large number of studies with inconsistent findings, but there is a suggestion that it may have more benefit for patients with vascular dementia than those with degenerative dementias [III]. It has no significant side effects [I].

A variety of other agents have been suggested as possibly helpful in the treatment of cognitive symptoms, some of the most promising of

which are under active study in clinical trials. Because these agents remain experimental, they are best taken in the context of a clinical trial. Such trials may be an appropriate option for some patients, since they offer the chance of clinical benefit while contributing to progress in treating dementia [III].

5. Treatment of psychosis and agitation

Psychosis and agitation are common in demented patients, often coexist, and may respond to similar therapies. In approaching any of these symptoms, it is critical to consider the safety of the patient and those around him or her [I]. The next step is a careful evaluation for a general medical, psychiatric, or psychosocial problem that may underlie the disturbance [I]. If attention to these issues does not resolve the problem and the symptoms do not cause undue distress to the patient or others, they are best treated with reassurance and distraction [I]. For agitation, some of the behavioral measures discussed in section I.B.2 may be helpful as well [II]. If other measures are unsuccessful, these symptoms may be treated judiciously with one of the agents discussed in the following paragraphs [II]. The use and need of such agents must be re-evaluated and documented on an ongoing basis [I].

Antipsychotics are the only documented pharmacologic treatment for psychosis in dementia [I] and are the best documented for agitation [II]. While they have been shown to provide modest improvement in behavioral symptoms in general [I], some research evidence, along with considerable anecdotal evidence, suggests that this improvement is greater for psychosis than for other symptoms [II]. There is no evidence of a difference in efficacy among antipsychotic agents [II]. The efficacy of these agents beyond 8 weeks has limited research support, but there is considerable clinical experience with this practice [II]. Antipsychotics have a number of potentially severe side effects, including sedation and worsening of cognition, and thus must be used at the lowest effective dose: extremely low starting doses are recommended for this population [I]. High-potency agents are more likely to cause akathisia and parkinsonian symptoms; low-potency agents are more likely to cause sedation, confusion, delirium, postural hypotension, and peripheral anticholinergic effects [I]. All conventional antipsychotic agents are also associated with more serious complications, including tardive dyskinesia (for which the elderly, women, and individuals with dementia are at greater risk) and neuroleptic malignant syndrome. Risperidone appears to share the risks associated with high-potency agents, although it may be somewhat less likely to cause extrapyramidal reactions [III]. Clozapine causes fewer extrapyramidal reactions, but it is associated with sedation, postural hypotension, and an elevated seizure risk and carries a risk of agranulocytosis, so it requires regular monitoring of blood counts [I]. The decision of which antipsychotic to use is based on the relationship between the side effect profile and the characteristics of a given patient [I]. It is expected that in the near future new agents that may alter decision making in this area will be

released, but they have not yet been tested with geriatric or demented populations, so they cannot be recommended at this time.

Benzodiazepines are most useful for treating patients with prominent anxiety or for giving on an as-needed basis to patients who have infrequent episodes of agitation or to individuals who need to be sedated for a procedure such as a tooth extraction [II]. Benzodiazepines appear to perform better than placebo but not as well as antipsychotics in treating behavioral symptoms, although the data are of limited quality [II]. They can have many side effects, including sedation, worsening cognition, delirium, an increase in the risk of falls, and worsening of sleep-disordered breathing [I]. It may be preferable to use lorazepam and oxazepam, which have no active metabolites and are not metabolized in the liver [III].

The anticonvulsant agents carbamazepine and valproate, the sedating antidepressant trazodone, the atypical anxiolytic buspirone, and possibly selective serotonin release inhibitors (SSRIs) are less well studied but may be appropriate for nonpsychotic patients with behavioral disorders, especially those with mild symptoms or sensitivity to antipsychotic medications. There is preliminary evidence to support their efficacy in the treatment of agitation [III]. Medroxyprogesterone and related hormones may have a role in the treatment of disinhibited sexual behavior in male patients with dementia [III]. Lithium and β blockers are not generally recommended: the few data supporting their use concern nondemented populations, and the potential side effects are serious [II].

6. Treatment of depression

Depression is common in patients with dementia. Patients with depression should be carefully evaluated for suicide potential [I]. Depressed mood may respond to improvements in the living situation or stimulation-oriented treatments [II], but patients with severe or persistent depressed mood with or without a full complement of neurovegetative signs should be treated with antidepressant medications [II]. Although formal evaluation of the efficacy of antidepressants for demented patients is limited, there is considerable clinical evidence supporting their use [II]. The choice among agents is based on the side effect profile and the characteristics of a given patient [I]. SSRIs are probably the first-line treatment, although one of the tricyclic antidepressants or newer agents, such as bupropion or venlafaxine, may be more appropriate for some patients [II]. Agents with significant anticholinergic effects (e.g., amitriptyline, imipramine) should be avoided [I]. Because of the elevated risk of dietary indiscretion in demented patients and the substantial risk of postural hypotension, monoamine oxidase inhibitors (MAOIs) are probably appropriate only for patients who have not responded to other treatments [II]. Although research data are limited, clinical experience suggests that electroconvulsive therapy (ECT) is effective in the treatment of patients who do not respond to other agents [II]. Twice-

rather than thrice-weekly and unilateral rather than bilateral treatments may decrease the risk of delirium or memory loss associated with this modality [III].

Treatments for apathy are not well documented, but psychostimulants, bupropion, bromocriptine, and amantadine may be helpful [III]. Psychostimulants are also sometimes useful in the treatment of depression in patients with significant general medical illness [III].

7. Treatment of sleep disturbances

Sleep disturbances are common in patients with dementia. Pharmacologic intervention should be considered only when other interventions, including careful attention to sleep hygiene, have failed [I]. If a patient has a sleep disturbance and requires medication for another condition, an agent with sedating properties, given at bedtime, should be selected if possible [II]. If the sleep disturbance does not coexist with other problems, possibly effective agents include zolpidem and trazodone [II], but there are few data on the efficacy of specific agents for demented patients. Benzodiazepines and chloral hydrate are usually not recommended for other than brief use because of the risk of daytime sedation, tolerance, rebound insomnia, worsening cognition, disinhibition, and delirium [II]. Triazolam in particular is not recommended because of its association with amnesia [II]. Diphenhydramine is generally not recommended because of its anticholinergic properties [II].

8. Special issues for long-term care

Many patients with dementia eventually require placement in a nursing home or other long-term care facility, and approximately two-thirds of nursing home patients suffer from dementia. Facilities should be structured to meet the needs of patients with dementia, including those with behavioral problems [I], which are extremely common. Staff with knowledge and experience concerning dementia and the management of noncognitive symptoms appear to be important [II]. Special care units may offer a model of optimal care for patients with dementia, although there is no evidence that special care units achieve better outcomes than traditional units [III].

A particular concern is the use of physical restraints and antipsychotic medications. When used appropriately, antipsychotics can relieve symptoms and reduce distress for patients and can increase safety for patients, other residents, and staff [I]. However, overuse can lead to worsening of the dementia, oversedation, falls, and tardive dyskinesia. Thus, federal regulations and good clinical practice require careful consideration and documentation of the indications and available alternatives, both initially and over time [I]. A dose decrease or discontinuation should be considered periodically for all patients who receive antipsychotic medications [I]. A structured education program for staff may decrease the use of these medications in nursing homes [II]. Physical restraints should be used only for patients who pose an

imminent risk of physical harm to themselves or others and only until more definitive treatment is provided or when other measures have been exhausted [I]. When restraints are used, the indications and alternatives should be carefully documented [I]. The need for restraints can be decreased by environmental changes that decrease the risk of falls or wandering and by careful assessment and treatment of possible causes of agitation [II].

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

To identify the type of evidence supporting the major recommendations in the full-text practice guide, each is keyed to one or more references and each reference is followed by a letter code in brackets that indicates the nature of the supporting evidence. Minor recommendations not keyed to references may be assumed to be based on expert opinion.

The bracketed letter following each reference indicates the nature of the supporting evidence, as follows:

[A] Randomized clinical trial. A study of an intervention in which subjects are prospectively followed over time; there are treatment and control groups.

[B] Clinical trial. A prospective study in which an intervention is made and the results of that intervention are tracked longitudinally; study does not meet standards for a randomized clinical trial.

[C] Cohort or longitudinal study. A study in which subjects are prospectively followed over time without any specific intervention.

[D] Case-control study. A study in which a group of patients is identified in the present and information about them is pursued retrospectively or backward in time.

[E] Review with secondary data analysis. A structured analytic review of existing data, e.g., a meta-analysis or a decision analysis.

[F] Review. A qualitative review and discussion of previously published literature without a quantitative synthesis of the data.

[G] Other. Textbooks, expert opinion, case reports, and other reports not included above.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Improved cognition

- Improved quality of life, mood, and behavior
- Maximized function in the context of existing deficits
- Treatment of, restoration of, and minimization of further decline of cognitive and functional losses associated with dementia; psychosis, anxiety, and agitation; depression and apathy; and sleep disturbances
- Assured safety and comfort of patients and their families in the context of living with difficult disease
- Decreased psychotic symptoms (including paranoia, delusions, and hallucinations) and associated or independent agitation, screaming, combativeness, or violence; and thereby increased comfort and safety of patients and their families and caregivers.

POTENTIAL HARMS

- Because elderly individuals are more likely to have a variety of general medical problems and take multiple medications, one must be alert to general medical conditions and medication interactions that may further alter the serum binding, metabolism, and excretion of the medication. In addition, certain medication side effects pose particular problems for elderly and demented patients, so medications with these effects must be used especially judiciously. Medications should be used with considerable care, and the use of multiple agents (sometimes referred to as "polypharmacy") should be avoided if possible.
- Side effects of psychosocial treatments: Short-term adverse emotional consequences have been reported with psychosocial treatments. This is especially true of the cognitively oriented treatments, during which frustration, catastrophic reactions, agitation, and depression have been reported.
- Side effects of pharmacologic therapy, including:
 - Side effects of cholinesterase inhibitors: nausea and vomiting are common, but tend to be mild to moderate for both agents. Additional cholinergic side effects include bradycardia, and increased gastrointestinal acid; these effects appear to occur infrequently. A unique property of tacrine is direct medication-induced hepatocellular injury.
 - Vitamin E has sometimes been noted to worsen blood coagulation defects in patients with vitamin K deficiency, and has been associated with an elevated rate of falls and syncope.
 - Selegiline's principal side effect is orthostatic hypotension. Other side effects include a somewhat higher rate of falls and syncope, and anxiety and/or irritability. Medication interactions include hypertensive crisis with an interaction with tyramine; and changes in mental status, seizure and even death have been observed with meperidine, SSRIs, and tricyclic antidepressants.
 - Ergoloid mesylates occasionally cause mild nausea or gastrointestinal distress; and is contraindicated with patients with psychosis.
 - Antipsychotic agents have a broad range of common side effects that tend to vary with medication potency. High-potency agents (e.g., haloperidol, fluphenazine) are most strongly associated with akathisia (which can worsen the target behaviors) and parkinsonian symptoms. Low-potency agents (e.g., thioridazine, chlorpromazine) are associated with sedation (which can lead to worsening cognition or falls),

confusion, delirium, postural hypotension (which can also lead to falls), and a variety of peripheral anticholinergic effects (e.g., dry mouth, constipation). Risperidone shares many features with high-potency antipsychotic agents. Clozapine is less commonly associated with extrapyramidal side effects but is associated with sedation, postural hypotension, and an elevated risk of seizures. More serious complications of antipsychotic agents include tardive dyskinesia and neuroleptic malignant syndrome. Clozapine has a significant risk of agranulocytosis.

- Benzodiazepines may be associated with sedation, ataxia, amnesia, delirium and paradoxical anxiety. These can lead to worsening cognition and behavior and can also contribute to the risk of falls. Benzodiazepines may also lead to disinhibition and medication dependence (and withdrawal).
- Anticonvulsants: the principal side effects of carbamazepine include ataxia, sedation, and confusion. In addition, in rare instances carbamazepine can lead to bone marrow suppression or hyponatremia. Valproate's principal side effects are gastrointestinal disturbances and ataxia. In addition, in rare instances it can lead to bone marrow suppression or hepatic toxicity.
- Antidepressants: SSRIs, including fluoxetine, paroxetine, and sertraline, tend to have a more favorable side effect profile than do cyclic agents. However, any SSRI can produce nausea and vomiting, agitation and akathisia, parkinsonian side effects, sexual dysfunction, and weight loss, although some of these effects are more common with one agent than another. In addition, physicians prescribing SSRIs should be aware of the many possible medication interactions. The structurally unique agent bupropion is associated with a risk of seizure, especially at high doses. Venlafaxine is associated with elevations in blood pressure, which sometimes diminish over time. Cyclic antidepressants generally have significant cardiovascular effects, including orthostatic hypotension and delays in cardiac conduction. Their effects on conduction make these agents dangerous in overdose. Most cyclic antidepressants have anticholinergic properties to some degree, including blurred vision, tachycardia, dry mouth, urinary retention, constipation, sedation, impaired cognition, and delirium. These effects are most marked for amitriptyline and imipramine and least so for nortriptyline and desipramine, but there is considerable variation from patient to patient. Trazodone has minimal cardiac conduction or anticholinergic effects but is associated with postural hypotension, sedation, and a risk of priapism. Nefazodone is most commonly associated with sedation. MAOIs, including tranylcypromine and phenelzine, can lead to postural hypotension; and they have complex medication interactions (sympathomimetic agents, narcotics, especially meperidine, and serotonergic agents must be avoided) and require dietary modifications (tyramine-containing foods, such as cheeses, preserved meat, and red wine, must be avoided). Psychostimulants (d-amphetamine, methylphenidate) are associated with tachycardia, restlessness agitation, sleep disturbances, and appetite suppression. Bromocriptine is associated with psychosis, confusion, and dyskinesias. Amantadine is sometimes associated with anticholinergic effects, including delirium.
- ECT is associated with the risk of cognitive side effects.

QUALIFYING STATEMENTS

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- This guideline is not intended to be construed or to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns evolve. These parameters of practice should be considered guidelines only. Adherence to them will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care aimed at the same results. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the psychiatrist in light of the clinical data presented by the patient and the diagnostic and treatment options available.
- This practice guideline has been developed by psychiatrists who are in active clinical practice. In addition, some contributors are primarily involved in research or other academic endeavors. It is possible that through such activities some contributors have received income related to treatments discussed in this guideline. A number of mechanisms are in place to minimize the potential for producing biased recommendations due to conflicts of interest. This guideline has been extensively reviewed by members of APA as well as by representatives from related fields. Contributors and reviewers have all been asked to base their recommendations on an objective evaluation of the available evidence. Any contributor or reviewer who has a potential conflict of interest that may bias (or appear to bias) his or her work has been asked to notify the APA Office of Research. This potential bias is then discussed with the work group chair and the chair of the steering Committee on Practice Guidelines. Further action depends on the assessment of the potential bias.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The American Psychiatric Association develops derivative products including patient guides, quick reference guides, and quality of care indicators with research studies to evaluate the effectiveness of the guideline.

IMPLEMENTATION TOOLS

Quick Reference Guides/Physician Guides
Staff Training/Competency Material

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

End of Life Care
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

American Psychiatric Association (APA). Practice guideline for the treatment of patients with Alzheimer's disease and other dementias of late life. Am J Psychiatry 1997 May; 154(5 Suppl): 1-39. [243 references] [PubMed](#)

American Psychiatric Association (APA). Practice guidelines for the treatment of patients with Alzheimer's disease and other dementias of late life. Washington (DC): American Psychiatric Press, Inc.; 1997 May. 93 p. [243 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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GUIDELINE DEVELOPER(S)

American Psychiatric Association - Medical Specialty Society

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GUIDELINE COMMITTEE

Work Group on Alzheimer's Disease and Related Dementias

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Names of Work Group Members: Peter Rabins, MD, MPH, Chair; Deborah Blacker, MD, ScD (Consultant); Walter Bland, MD; Lory Bright-Long, MD; Eugene Cohen, MD; Ira Katz, MD; Barry Rovner, MD; Lori Schneider, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

This practice guideline has been developed by psychiatrists who are in active clinical practice. In addition, some contributors are primarily involved in research or other academic endeavors. It is possible that through such activities many contributors have received income related to treatments discussed in this guideline. A number of mechanisms are in place to minimize the potential for producing biased recommendations due to conflicts of interest. The guideline has been extensively reviewed by members of American Psychiatric Association (APA) as well as by representatives from related fields. Contributors and reviewers have all been asked to base their recommendations on an objective evaluation of the available evidence. Any contributor or reviewer who has a potential conflict of interest that may bias (or appear to bias) his or her work has been asked to notify the APA Office of Research. This potential bias is then discussed with the work group chair and the chair of the Steering Committee on Practice Guidelines. Further action depends on the assessment of the potential bias.

GUIDELINE STATUS

This is the current release of the guideline.

According to the guideline developer, this guideline is still considered to be current as of December 2004, based on a review of literature published since the original guideline publication.

In addition, a Guideline Watch, which summarizes significant developments in practice since the publication of the original guideline, was published in August 2004 and is available from the [American Psychiatric Association Web site](#) (see also the "Availability of Companion Documents" field below).

GUIDELINE AVAILABILITY

Electronic copies: Available from the [American Psychiatric Association \(APA\) Web site](#).

Print copies: Available from the American Psychiatric Press, Inc (APPI), 1000 Wilson Boulevard, Suite 1825, Arlington, VA 22209-3901; (703) 907-7322; (800) 368-5777; fax (703) 907-1091.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- American Psychiatric Association practice guideline development process. In: Practice Guidelines for the Treatment of Psychiatric Disorders: Compendium 2000. Washington, DC: APA, 2000.

- Treating Alzheimer's disease and other dementias of late life: A quick reference guide. Washington, DC: American Psychiatric Association. 14 p. Electronic copies: Available in Portable Document Format (PDF) from the [American Psychiatric Association Web site](#).
- Rabins PV. Guideline watch: practice guideline for the treatment of patients with Alzheimer's disease and other dementias of late life. Arlington (VA): American Psychiatric Association; 2004 Aug. 6 p. Electronic copies available in Portable Document Format (PDF) from the [American Psychiatric Association Web site](#).

Print copies: Available from the American Psychiatric Press, Inc (APPI), 1000 Wilson Boulevard, Suite 1825, Arlington, VA 22209-3901; (703) 907-7322; (800) 368-5777; Fax (703) 907-1091.

Additionally, a continuing medical education (CME) course is available online at the [American Psychiatric Association Web site](#).

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on December 1, 1998. The information was verified by the guideline developer on January 11, 1999. This summary was most recently updated by ECRI on April 15, 2005 following the public health advisory concerning an unapproved "off-label" use of atypical antipsychotic drugs in elderly patients with dementia. This summary was updated by ECRI on August 15, 2005, following the U.S. Food and Drug Administration advisory on antidepressant medications. This summary was updated by ECRI on January 18, 2006, following the U.S. Food and Drug Administration advisory on Clozaril (clozapine).

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